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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 12/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/942,052	RAITANO ET AL.	
	Examiner	Art Unit	
	David J Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-72* is/are pending in the application.

4a) Of the above claim(s) *1-3,7-13,22,25-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6,14-21,23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2/11/2003* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group III, claims 4-6, 14-21, 23, 24, 46, 48, 54 and 56, filed 9/22/2003 is acknowledged. Upon further consideration the restriction requirement mailed 7/15/2003 grouped patentably distinct product claims with patentably distinct method claims in Groups II-VIII. Therefore the restriction requirement mailed 7/15/2003 is vacated and a new restriction requirement follows.

2. Applicant is advised that multiple elections may be required in this restriction requirement (see items 6, 7 and 10 below).

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-3, drawn to a method for monitoring 85P1B3 gene products in a biological sample from a patient who has or who is suspected of having cancer, classified in class 435, subclasses 6, 7.1, for examples.

II. Claims 4-6 in part and claims 7-12, drawn to a composition comprising a substance that modulates the status of 85P1B3, wherein the substance comprises a 85P1B3-related protein, classified in class 424, subclass 184.1.

III. Claims 46 and 54 in part and claim 55, drawn to methods for inhibiting the growth of cancer cells and treating a patient who bears cancer cells expressing 85P1B3 with a substance that modulates the status of 85P1B3, wherein the substance comprises a 85P1B3-related protein, classified in class 530, subclass 350.

IV. Claims 4-6 in part and claims 14-21 and 23-24, drawn to a composition comprising a substance that modulates the status of 85P1B3, wherein the substance comprises an antibody that binds to a 85P1B3-related protein, and a hybridoma that produces the same antibody, classified in class 530, subclass 387.1.

V. Claims 46 and 54 in part and claims 48 and 56, drawn to methods of inhibiting the growth of cancer cells and treating a patient bearing cancer cells that express 85P1B3 with a substance that modulates the status of 85P1B3, wherein the substance comprises an antibody that binds to a 85P1B3-related protein, classified in class 424, subclass 130.1

VI. Claims 4-6 in part and claims 25 and 27, drawn to a composition comprising a substance that modulates the status of 85P1B3, wherein the substance comprises a polynucleotide that encodes a single chain antibody that binds to a 85P1B3-related protein, and a vector comprising such, classified in class 514, subclass 44.

VII. Claims 46 and 54 in part and claims 49, 54 and 57-58, drawn to methods for inhibiting the growth of cancer cells and treating a patient bearing

cancer cells expressing 85P1B3 with a substance that modulates the status of 85P1B3, wherein the substance comprises a polynucleotide that encodes a single chain antibody that binds to a 85P1B3-related protein, and a vector comprising such, classified in class 536, subclass 23.53.

VIII. Claims 4-6 in part and claims 13 and 28-36, drawn to a composition comprising a substance that modulates the status of 85P1B3, wherein the substance comprises a polynucleotide that comprises an 85P1B3-related protein coding sequence, classified in class 514, subclass 44.

IX. Claims 46 and 54 in part and claims 50 and 59, drawn to methods for inhibiting the growth of cancer cells and treating a patient bearing cancer cells expressing 85P1B3 with a substance that modulates the status of 85P1B3, wherein the substance comprises a polynucleotide that comprises an 85P1B3-related protein coding sequence, classified in class 536, subclass 23.5.

X. Claims 4-6 in part and claims 37-43, drawn to a composition comprising a substance that modulates the status of 85P1B3, wherein the substance comprises a polynucleotide that is fully complementary to a polynucleotide that comprises an 85P1B3–related protein coding sequence, classified in class 514, subclass 44.

XI. Claims 46 and 54 in part and claims 51 and 60, drawn to methods for inhibiting the growth of cancer cells and treating a patient bearing cancer cells expressing 85P1B3 with a substance that modulates the status of

85P1B3, wherein the substance comprises a polynucleotide that is fully complementary to a polynucleotide that comprises an 85P1B3–related protein coding sequence, classified in class 536, subclass 24.2.

XII. Claims 4-6 in part and claims 44, drawn to a composition comprising a substance that modulates the status of 85P1B3, wherein the substance comprises a ribozyme that cleaves a polynucleotide having the 85P1B3 coding sequence, classified in class 514, subclass 44.

XIII. Claims 46 and 54 in part and claims 44, 52 and 61, drawn to methods for inhibiting the growth of cancer cells and treating a patient bearing cancer cells expressing 85P1B3 with a substance that modulates the status of 85P1B3, wherein the substance comprises a ribozyme that cleaves a polynucleotide having the 85P1B3 coding sequence, classified in class 536, subclass 24.5.

XIV. Claims 4-6 in part and claim 45, drawn to a composition comprising a substance that modulates the status of 85P1B3, wherein the substance comprises human T cells wherein the T cells specifically recognize an 85P1B3 peptide sequence in the context of a particular HLA molecule, methods for inhibiting growth or treating a patient who bears cancer cells expressing 85P1B3 using the same, and a composition comprising the same human T cells, classified in class 424, subclass 93.71.

XV. Claims 46 and 54 in part and claims 53 and 62, drawn to methods for inhibiting the growth of cancer cells and treating a patient bearing cancer

cells expressing 85P1B3 with a substance that modulates the status of 85P1B3, wherein the substance comprises human T cells wherein the T cells specifically recognize an 85P1B3 peptide sequence in the context of a particular HLA molecule, classified in class 435, subclass 325.

XVI. Claims 63-67 in part, drawn to a method of generating a mammalian immune response directed to 85P1B3, the method comprises exposing cells of the mammal's immune system to an immunogenic portion of an 85P13-related protein, whereby an immune response is generated to 86P1B3, classified in class 424, subclass 184.1.

XVII. Claims 63-67 in part, drawn to a method of generating a mammalian immune response directed to 85P1B3, the method comprises exposing cells of the mammal's immune system to a nucleotide sequence that encodes a 85P13-related protein, whereby an immune response is generated to 86P1B3, classified in class 514, subclass 44.

XVIII. Claims 68 and 70 in part and claim 69, drawn to an assay for detecting the presence of an 85P1B3-related protein in a biological sample from a patient who has or who is suspected of having cancer using an antibody that specifically binds to the 85P1B3-related protein, classified in class 435, subclass 7.1.

XIX. Claims 68 and 70 in part and claim 71, drawn to an assay for detecting the presence of an 85P1B3-related polynucleotide in a biological sample from a patient who has or who is suspected of having cancer using a

polynucleotide probe that specifically hybridizes to a polynucleotide encoding an 85P1B3-related protein having the amino acid sequence of Figure 2, classified in class 435, subclass 6.

XX. Claim 68 in part and claim 72, drawn to an assay for detecting the presence of 85P1B3 mRNA in a biological sample from a patient who has or who is suspected of having cancer using RT-PCR approach, classified in class 435, subclass 91.2.

XXI. Claim 22, drawn to a non-human transgenic animal that produces an antibody that specifically binds to a 85P1B3-related protein, classified in class 800, subclass 4.

3. Claims 4-6 link inventions II-XV. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 4-6. Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicants are advised that if any such claims depending from or including all the limitations of the allowable linking claims are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the

provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

4. Claims 63-67 link inventions XVI-XVII. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claims, claims 63-67. Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicants are advised that if any such claims depending from or including all the limitations of the allowable linking claims are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

5. Claim 68 link inventions XVIII-XX. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim, claim 68. Upon the allowance of the linking claim, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claim will be entitled to examination in the instant application. Applicants are advised that if any such claims depending from or including all the limitations of the allowable linking claim is presented in a continuation or

divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

6. Additionally, should Applicants elect the invention of Group II or III, **further group restriction** is required. This is because the CTL polypeptide epitopes selected from Tables V-XVIII containing 700 different SEQ ID Nos., have distinct amino acid sequences that have no substantial common core structure among themselves and they also have different biological activities. As set forth in MPEP 803.02, unity of invention exists if all species recited in a claim (1) shows a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility. Accordingly, Applicant is required to elect a specific CTL polypeptide epitope selected from Tables V-XVIII.

7. Additionally, should Applicants elect the invention of Group VIII or IX, **further group restriction** is required. This is because a polynucleotide that encodes at least one peptide selected from Tables V-XVIII containing 700 different SEQ ID NOs., wherein each encoded peptide has a distinct amino acid sequence having no substantial common core structure one from the others and each encoded peptide also has a different biological activity. As set forth in MPEP 803.02, unity of invention exists if all species recited in a claim (1) shows a common utility, and (2) share a substantial

structural feature disclosed as being essential to that utility. Accordingly, Applicant is required to elect a polynucleotide that encodes at least a specific peptide from Tables V-XVIII.

8. The inventions are distinct, each from the other because of the following reasons: The methods of Groups I, III, V, VII, IX, XI, XIII, XV and XVI-XX differ in the method steps and parameters and in the reagents used. Invention I recites a method for monitoring 85P1B3 gene products in a biological sample from a patient who has or who is suspected of having cancer; Invention III recites a method for inhibiting the growth of cancer cells and treating a cancer patient with a 85P1B3-related protein; Invention V recites a method for inhibiting the growth of cancer cells and treating a cancer patient with an antibody that binds 85P1B3; Invention VII recites a method for inhibiting the growth of cancer cells and treating a cancer patient with a polynucleotide that encodes a single chain antibody that binds to a 85P1B3-related protein; Invention IX recites a method for inhibiting the growth of cancer cells and treating a cancer patient with a polynucleotide that comprises an 85P1B3-related protein coding sequence; Invention XI recites a method for inhibiting the growth of cancer cells and treating a cancer patient with a polynucleotide that is fully complementary to a polynucleotide that comprises an 85P1B3–related protein coding sequence; Invention XIII recites a method for inhibiting the growth of cancer cells and treating a cancer patient with a ribozyme that cleaves a polynucleotide having the 85P1B3 coding sequence; Invention XV recites a method for inhibiting the growth of cancer cells and treating a cancer patient with human T cells wherein the T cells specifically recognize an 85P1B3 peptide sequence in the context of

a particular HLA molecule; Invention XVI recites a method for inhibiting the growth of cancer cells and treating a cancer patient with an immunogenic portion of an 85P13 related protein; Invention XVII recites a method of generating a mammalian immune response directed to 85P1B3 with a nucleic acid sequence that encodes a 85P1B3-related protein; Invention XVIII recites an assay for detecting the presence of an 85P1B3-related protein in a biological sample from a patient who has or who is suspected of having cancer using an antibody that specifically binds to the 85P1B3-related protein; Invention XIX recites an assay for detecting the presence of an 85P1B3-related polynucleotide in a biological sample from a patient using a polynucleotide that hybridizes to a polynucleotide encoding an 85P1B3-related protein having the amino acid sequence of Figure; Invention XX recites an assay for detecting the presence of 85P1B3 mRNA in a biological sample from a patient using RT-PCR. The examination of all groups would require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus, Inventions I, III, V, VII, IX, XI, XIII, XV and XVI-XX are separate and distinct in having different method steps, parameters, reagents used and different endpoints and are patentably distinct.

Inventions of Groups II, IV, VI, VIII, X, XII, XIV and XXI represent separate and distinct products which are made by materially different methods, and are used in materially different methods which have different modes of operation, different functions and different effects. The polynucleic acid of Groups VI, VIII and X, the protein product of Groups II and XII and the antibody of Group IV are all structurally and chemically

different from each other. The polynucleotide is made by nucleic acid synthesis, while the polypeptide is made by translation of mRNA, the antibody is raised by immunization. Furthermore, the polynucleotide can be used for hybridization screening, the polypeptide can be used for methods of treatment, the antibody can be used to immunopurify the antigen, for example. Additionally, the human cells of Group XIV and the non-human transgenic animal of Group XXI are functionally distinct products having different effects. The examination of all groups would require different searches in the U.S. Patent shoes and the scientific literature and would require the consideration of different patentability issues. Thus, the inventions of Groups II, IV, VI, VIII, X, XII, XIV and XXI are patentably distinct.

Inventions II and III, XVI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the substance comprising an 85P1B3-related protein can be used in methods of inhibiting cancer growth or treating a patient who bears cancer cells of Group III or in a method of generating a mammalian immune response directed against 85P1B3 of Group XVI.

Inventions IV and V, XVIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different

process of using that product (MPEP § 806.05(h)). In the instant case the substance comprising an antibody that specifically binds to a 85P1B3-related protein can be used either in methods of inhibiting cancer growth or treating a patient who bears cancer cells of Group V or in an assay for detecting the presence of an 85P1B3-related protein in a biological sample of Group XVIII.

Inventions VI and VII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polynucleotide encoding a single-chain antibody that binds to a 85P1B3-related protein can be used to make the single-chain antibody and purify the antigen.

Inventions VIII and IX, XVII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polynucleotide encoding the 85P1B3-related protein can be used either in methods of inhibiting cancer growth or treating a patient who bears cancer cells of Group IX or generating a mammalian immune response directed to 85P1B3 of Group XVII.

Inventions X and XI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the

process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polynucleotide that is fully complementary to a polynucleotide that comprises an 85P1B3–related protein coding sequence can be used to diagnose cancer in addition to the materially different method of Group XI.

The different inventions above have acquired a separate status in the art as a separate subject for inventive effect and require independent searches. The search for each of the above inventions is not co-extensive particularly with regard to the literature search. Additionally, because of limited resources from the USPTO to conduct the computer search of the claimed SEQ ID Nos. listed in Tables V-XVIII, and all of the SEQ ID Nos. not possess a common core structure or element, an undue burden would be needed to search and examine all of the claimed inventions in a single application, restriction for examination purposes as indicated is proper.

9. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

10. ***Species restriction***

A. Should Applicants elect Group I, claims 1-3 are generic to a plurality of disclosed distinct species comprising:

A specifically named cancer set forth in Table 1 as recited in claim 3.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

B. Should Applicants elect either Group XVI or Group XVII, claims 63-64 are generic to a plurality of disclosed distinct species comprising:

(a) a T cell epitope, or (b) a B cell epitope.

Applicant is required under 35 U.S.C. 121 to elect a specifically named species as indicated above.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the grounds that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over

the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

11. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised

that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

12. During a telephone conversation with Robert K. Cerpa on 12/3/2003 a provisional election was made with traverse to prosecute the invention of Group IV, claims 4-6, 14-21 and 23-24 drawn to drawn to a composition comprising a substance that modulates the status of 85P1B3, wherein the substance comprises an antibody that binds to a 85P1B3-related protein, and a hybridoma that produces the same antibody.

Applicant's election with traverse of Group III (Renumbered as Group IV in the instant restriction requirement) in the paper filed 9/22/2003 is acknowledged. The traversal is on the grounds that a prior art search of former Groups III and IV or current Groups IV and VI would not impose a serious burden on the examiner. The traversal further states that a search describing the nucleic acid encoding an antibody would reveal references describing the antibody encoded by the nucleic acid and a search for art directed to the antibody will also encompass art describing how the antibody was made. A search of the nucleic acid or antibody would be overlapping and thus, would not impose a serious burden on the examiner. This is not found persuasive. The inventions are distinct because as stated in the restriction requirement the nucleic acids and antibodies are structurally and functionally distinct. Further, art teaching an

antibody would not necessarily teach how the antibody was made, particularly if the antibody was made and taught in an earlier publication.

As to the question of burden of search, the antibody of Group III (now Group IV) is classified in class 424, subclass 130.1, while the polynucleotide of Group IV (now Group VI) is classified in class 514, subclass 44. The divergent classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and different patentability issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is made FINAL.

13. Affirmation of this election must be made by applicant in replying to this Office action.

14. Claims 1-3, 7-13, 22 and 25-72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

15. Claims 4-6, 14-21 and 23-24 are under examination.

Specification

16. The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. For example, on page 6, lines29 and 33.

Applicant is required to check the entire disclosure and delete all the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Oath/Declaration

17. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application-by-application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
There are non-initialed and/or non-dated alterations have been made to the declaration under inventor Arthur B. Raitano. The address has been altered. See 37 CFR 1.52(c).

Claim Objections

18. Claims 4 are objected to because of the following informalities:

Claim 4 is broadly drawn to non-elected inventions. Claim 4 recites a "substance" which encompasses other embodiments other than the elected antibody that binds to a 85P1B3-related protein.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

20. Claims 4-6, 14-21 and 23-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

a) Claim 4 and those claims that depend from claim 4 are indefinite for reciting "modulates the status of 85P1B3" in claim 4. It is unclear what is contemplated by the phrase "modulates the status of 85P1B3". First, it is unclear whether the "substance" "modulates the status of 85P1B3" gene or protein. Second, does the "substance "modulate the status of 85P1B3" by up- or down-regulating 85P1B3 gene expression or is the substance intended to "modulate" 85P1B3 protein activity? If the substance is intended to "modulate" 85P1B3 protein activity, what activity is modulated and what is the nature of the modulation? Does the substance "modulate" a catalytic activity of the 85P1B3 protein or does the substance inhibit/enhance the binding or association of the 85P1B3 protein with its binding partner or with other proteins for example?

b) Claim 4 and those claims that depend from claim 4 are indefinite for reciting "a molecule that is modulated by 85P1B3" in claim 4. It is unclear what is contemplated by the phrase "a molecule that is modulated by 85P1B3". It is unclear how the 85P1B3 modulates a molecule and how that modulation relates to the status of a cell that expresses 85P1B3. Does the 85P1B3 gene or protein "modulate" a molecule that alters

the status of a cell that expresses 85P1B3 and how is the status of a cell expressing 85P1B3 "modulated"?

c) Claim 6 is indefinite for reciting "human unit dose form". The phrase ""human unit dose form" is not one, which has a universally accepted meaning in the art nor is it one which has been adequately defined in the specification. The primary deficiency in the use of this phrase is the absence of an ascertainable meaning for said phrase. The phrase "human unit dose form" can encompass different dosage regimens, different concentrations or different time points for administration or any combination thereof. In the absence of a single defined art recognized meaning for the phrase "human unit dose form" and lacking a definition of the phrase in the specification, one of ordinary skill in the art could not determine the metes and bounds of the claims.

d) Claim 14 and those claims that depend from claim 14 are indefinite for reciting "antibody or fragment thereof that specifically binds to a 85P1B3-related protein". It is unclear whether or not the antibody binds the 85P1B3 protein disclosed as SEQ ID NO: 728. Does the antibody bind SEQ ID NO: 728 (85P1B3) or does the antibody only bind "85P1B3-related proteins"?

Claim Rejections - 35 USC § 112

21. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

22. Claims 4-6, 14-21 and 23-24 are rejected under 35 U.S.C. as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This is a written description rejetion.

The specification discloses the 85P1B3 polynucleotide (SEQ ID NO: 727; Figure 2) and the 85P1B3 polypeptide (SEQ ID NO: 728; Figure 3) but the specification does not disclose 85P1B3-related proteins, which are disclosed as comprising allelic variants, conservative substitution variants, analogs, homologs and fusion proteins that "combine parts of different 85P1B3 proteins or fragments thereof" (see page 16, line28-32 and pages 24-27).

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Thus, the instant specification may provide an adequate written description of the 85P1B3-related proteins, by structurally describing a representative number of 85P1B3-related proteins that cross-react with the anti-85P1B3 antibody or by describing structural features common to the members of the genus, which features constitute a substantial portion of the genus. Alternatively, the specification can show that the claimed invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of characteristics.

In the instant case, the specification does not describe the 85P1B3-related proteins required to practice the claimed invention. The specification does not provide the complete structure of any 85P1B3-related protein, nor does the specification provide any partial structure of such 85P1B3-related proteins, nor any physical or chemical characteristics of the 85P1B3-related proteins, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. The specification also does not describe the 85P1B3-related proteins to which the anti-85P1B3 antibodies bind. The specification describes only a single 85P1B3 polypeptide (SEQ ID NO: 728) and thus, it does not describe a representative number of species. Additionally, the specification does not describe structural features common to the members of the genus, which features constitute a substantial portion of the genus.

The general knowledge in the art concerning variants does not provide any indication of how the structure of one variant is representative of unknown variants. Reiger et al. (Glossary of Genetics and Cytogenetics, Classical and Molecular, 4th Ed., Springer-Verlay, Berlin, 1976) clearly define alleles as one of two or more alternative forms of a gene occupying the same locus on a particular chromosome... and differing from other alleles of that locus at one or more mutational sites (page 17). Thus, the structure of naturally occurring allelic sequences are not defined. The skilled artisan cannot envision the detailed structure of the encompassed 85P1B3-related polypeptides and therefore, conception is not achieved until reduction to practice has occurred.

Thus, one of skill in the art would not understand that the applicant had possession of the claimed invention at the time the instant application was filed.

23. Claims 4-6, 14-21 and 23-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the 85P1B3 polypeptide and antibodies that bind the 85P1B3 protein (SEQ ID NO: 728), does not reasonably provide enablement for 85P1B3-related protein variants, or antibodies that bind 85P1B3-related protein variants, or using pharmaceutical compositions comprising a substance that modulates the status of 85P1B3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to a substance that modulates the status of 85P1B3, or a molecule that is modulated by 85P1B3 whereby the status of a cell that expresses 85P1B3 is modulated and an antibody that specifically binds the 85P1B3-related protein and pharmaceutical compositions comprising such.

The specification teaches that the 85P1B3 mRNA is expressed in numerous human cancer cell lines (see Fig 12) and in some cancer patient specimens including

breast, prostate, uterus, cervix, stomach, lung, colon and bladder cancers (see Figures 13-16). The specification also teaches 85P1B3 specific antibodies that are reactive against the 85P1B3 (see Figure 20).

The specification does not teach that the 85P1B3 protein or 85P1B3-related mRNA's or proteins are expressed in cancer cells or cancer patients or whether 85P1B3-specific antibodies cross-react with 85P1B3-related proteins.

The specification does not reasonably provide enablement for 85P1B3-related protein variants, or antibodies that bind 85P1B3-related protein variants, or pharmaceutical compositions comprising such based on the written disclosure alone. Those of skill in the art recognize that expression of mRNA, specific for a tissue type, does not necessarily correlate nor predict equivalent levels of polypeptide expression. In fact, evidence abounds in which protein levels do not correlate with steady-state mRNA levels or alterations in mRNA levels. For example, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Further, Powell et al (Pharmacogenetics, 1998, Vol. 8, pp. 411-421, abstract) teach that mRNA levels for cytochrome P450 E1 did not correlate with the level of corresponding protein, and conclude that the regulation of said protein is highly complex. Vallejo et al (Biochimie, 2000, vol. 82, pp. 1129-1133, abstract) teach that no correlation was found between NRF-2 mRNA and protein levels suggesting post-transcriptional regulation of NRF-2 protein levels. These references serve to demonstrate that the analysis of levels

of polynucleotide transcripts cannot be relied upon to anticipate levels of protein expression. Further, Jang et al (Clinical and Experimental Metastasis, 1997, vol. 15, pp. 469-483, abstract) teach that further studies are necessary to determine if changes in protein levels track with changes in mRNA levels for metastasis associated genes in murine tumor cells, thus providing further evidence that one of skill in the art cannot anticipate that the level of a specific mRNA expressed by a cell will be paralleled at the protein level due to complex homeostatic factors controlling translation and post-translational modification.

Thus, the predictability of protein translation and its possible utility as a diagnostic or therapeutic target are not necessarily contingent on the levels of mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Therefore, absent evidence of the 85P1B3 and 85P1B3-related protein expression, including the correlation to a diseased state, one of skill in the art would not be able to predictably use antibodies that bind the 85P1B3 polypeptide or 85P1B3-related polypeptides in pharmaceutical compositions as a diagnostic or therapeutic tool. The specification does not predict or show whether the 85P1B3 polypeptide or 85P1B3-related polypeptides would be overexpressed or under expressed in a specific, diseased tissue compared to the healthy tissue control. In the absence of a direct correlation between the up regulation of transcription and translation of the 85P1B3 polypeptide or 85P1B3-related polypeptides associated with a disease state, one of ordinary skill in the art would be unable to use antibodies specific for the 85P1B3

polypeptide or antibodies specific for 85P1B3-related polypeptides in pharmaceutical compositions.

The specification does not disclose the extremely large number of proteins broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species as in the case of 85P1B3-related polypeptide sequences that may comprise nonfunctional proteins or proteins that are not reactive with the 85P1B3-specific antibodies. Coleman P. M. (Research in Immunology. 145: 33-36, 1994) teach the uncertainty surrounding amino acid changes related to antibody-antigen complex formation. Single amino acid changes within the antibody-antigen interface have the capacity to drive the affinity towards more tightly bound complexes or such changes in the antigen can effectively abolish the interaction entirely (see pages 33-34). Applicants have not disclosed any 85P1B3-related sequences that are expected to cross-react with the disclosed 85P1B3 specific antibodies or what structural changes to the 85P1B3 protein can be made without altering function and antibody reactivity. The claims broadly encompass yet to be discovered 85P1B3-related proteins of unknown function and without the direct association of any 85P1B3-related protein to a tumorous or cancerous disease state or other disease, one of skill in the art would not know how to use antibodies that bind 85P1B3-related proteins.

No direction or guidance is provided to assist one skilled in the art to make and use the claimed antibodies that bind 85P1B3-related polypeptides in order to modulate the status of 85P1B3 in a manner reasonably correlated with the scope of the claims.

The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970).

In view of the lack of predictability of the art to which the invention pertains as evidenced by Fu et al., Powell et al., Vallejo et al., Jang et al., and Coleman P. M. and lack of guidance in the specification related to using antibodies that specifically react with 85P1B3-related proteins for modulating the status of 85P1B3, undue experimentation would be required to practice the claimed antibodies as a pharmaceutical composition with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed invention and absent working examples providing evidence which is reasonably predictive that the claimed pharmaceutical composition is effective for modulating the status of 85P1B3.

Claim Rejections - 35 USC § 102

24. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

25. Claims 4-6,14-21 and 23-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang Y. T. et al (WO 01/53312, 102(e) date 1/21/2000, Ids filed 2/11/2003).

The claims recite a pharmaceutical composition comprising an antibody that specifically binds an 85P1B3-related protein and modulates the status of 85P1B3, or a molecule that is modulated by 85P1B3 whereby the status of a cell that expresses 85P1B3 is modulated and the antibody is labeled with a detectable marker. Due to the indefinite nature of the claims (see 112, 2nd above), the claims are interpreted to mean that the antibody binds the 85P1B3 protein.

Tang et al teach two polypeptides (SEQ ID NO: 3368 and SEQ ID NO: 6940) that share 100% amino acid identity with the disclosed 85P1B3 polypeptide (SEQ ID NO:728) (see alignments attached to this office action). Tang et al teach pharmaceutical compositions (pages 63-71), effective dosages (pages 72-73), and antibodies that bind the polypeptides sharing 100% amino acid identity with the 85P1B3 protein, including polyclonal antibodies, monoclonal antibodies, humanized antibodies, human antibodies, Fab fragments, single-chain antibodies and bispecific antibodies (see pages 74-83) and labeling the antibodies for diagnostic assays (see pages 87-88). Tang et al also teach hybridoma production for making antibodies that bind the polypeptides disclosed as SEQ ID NO: 3368 and 6940) (see pages 76-77).

Conclusion

26. No claim is allowed.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number through January 19, 2004 is (703) 605-1200. The examiner can be reached at (571) 272-0827 beginning January 21, 2004. The examiner can normally be reached at (703) 605-1200 from 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, can be reached at (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1123.

Official papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The official fax number for Group 1600 where this application or proceeding is assigned is (703) 872-9306.

Respectfully,
David J. Blanchard
703-605-1200

LARRY R. HELMS, PH.D
PRIMARY EXAMINER